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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/772,996

02/05/2004

Shiv Kumar

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5385

7590 09/07/2007
Amersham Biosciences Corp
800 Centennial Avenue
Piscataway, NJ 08855

EXAMINER

BABIC, CHRISTOPHER M

ART UNIT	PAPER NUMBER
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1637

MAIL DATE	DELIVERY MODE
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09/07/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/772,996	Applicant(s) KUMAR ET AL.	
	Examiner Christopher M. Babic	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 May 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 and 4-12 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1 and 4-12 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the Claims

Claim(s) 1 and 4-12 are pending. The following Office Action is in response to Applicant's response dated May 29, 2007.

Withdrawn Claim Rejections - 35 USC § 112 - Indefiniteness

The rejection of claim(s) 4 has been withdrawn in view of Applicant's amendment.

Withdrawn Claim Rejections - 35 USC § 112 - New Matter

The rejection of claim(s) 5-7 has been withdrawn in view of Applicant's amendment.

Withdrawn Claim Rejections - 35 USC § 112 - Written Description

The rejection of claim(s) 1 and 5-12 has been withdrawn in view of Applicant's amendment.

Withdrawn Claim Rejections - 35 USC § 112 - Scope of Enablement

The rejection of claim(s) 1-12 has been withdrawn in view of Applicant's amendment.

Withdrawn Claim Rejections - 35 USC § 102

The rejection of claim(s) 1, 3, 5, and 7 over Yarbrough has been withdrawn in view of Applicant's amendment.

Withdrawn Claim Rejections - 35 USC § 103

The rejection of claim(s) 1, 3, and 5-10 over Wu in view of Bernard and Yarbrough has been withdrawn in view of Applicant's amendment.

Maintained Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim(s) 1, 4-7, 11, and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hardin (U.S. 2003/0064366 A1) in view of McGuigan et al. ("DNA fingerprinting by sampled sequencing" Methods Enzymol. 1993;218:241-58).

With regard to claim(s) 1, Hardin teaches a method (pg. 31, col. 1, for example) comprising: a) conducting said enzyme catalyzed nucleoside monophosphate transfer from a terminal-phosphate-labeled nucleoside polyphosphate reaction in reaction buffer (pg. 31, col. 1, for example); wherein said enzyme is selected from a template dependent nucleic acid polymerase (pg. 31, col. 1, Sequenase, for example). Hardin further teaches gamma-phosphate labeled ddNTPs ([0244], for example).

Hardin does not expressly teach a reaction buffer comprising magnesium.

McGuigan provides a supporting disclosure that teaches that upon the addition of manganese ions to a Sequenase reaction system, i.e. **a sequencing reaction with dNTPs and ddNTPs present**, the polymerase incorporates ddNTPs at a greater rate (pg. 247, Enzymes, for example).

With regard to claim(s) 4, McGuigan teaches Sequenase (pg. 253, for example).

With regard to claim(s) 5-7, McGuigan teaches a manganese salt concentration of 5mM (pgs. 251 and 253, 1X conc., for example).

With regard to claims 11 and 12, McGuigan teaches EDTA within the reaction mixture (pgs. 252 and 253, steps 9 and 10, for example).

It is clear from the teachings of Bernard that one of ordinary skill in the art would have been motivated to add manganese ions to the methods of Hardin to increase the rate of ddNTP incorporation thus effectively increasing the incorporation of terminal-phosphate-labeled nucleotides, however, as discussed in the above enablement rejection, one of ordinary skill in the art, absent an express teaching, cannot accurately

predict the biochemical behavior of a polymerase within the presence of manganese and/or terminal phosphate-labeled nucleotides.

Though, in the case of Sequenase, it was known that Sequenase was able to incorporate terminal phosphate-labeled nucleotides as demonstrated by Hardin. Thus, there was a reasonable expectation of success at the time of invention.

Therefore, it would have been *prima facie obvious* to a skilled artisan at the time of invention to incorporate manganese ions into the methods of Hardin since McGuigan suggests such a modification to increase the rate of incorporation of ddNTP incorporation, thus arriving at the claimed invention.

Response to Arguments

Applicant's arguments have been fully considered but they are not persuasive.

First, Applicant argues that McGuigan, as evidenced by Tabor and Richardson, teaches that manganese causes a rate decrease in incorporation of dNTPs by Sequenase. Thus, a skilled artisan could not have reached the conclusion that in the presence of manganese, the polymerase incorporates ddNTPs at a greater rate. This argument is not persuasive because Applicant is claiming an **increase in the rate of reaction**, which would necessarily occur within a sequencing reaction (e.g. Sequenase with dNTPs and ddNTPs) that contains a polymerase with a rate decrease in incorporation of dNTPs as opposed to ddNTPs. In other words, a reaction that contains dNTPs and ddNTPs, i.e. two different substrates, with a polymerase that has an increased discrimination for dNTPs, i.e. one substrates, will necessarily contain a

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polymerase that incorporates ddNTPs, i.e. the different substrate, more often.

Applicant is correct in asserting that Tabor and Richardson demonstrate that when both ddNTPs and dNTPs are present, manganese increases the relative incorporation of ddNTPs by Sequenase, i.e. in the presence of manganese, Sequenase will incorporate more ddNTPs in the same amount of time over the same reaction in the absence of manganese, because Sequenase will attach to ddNTPs more often in the presence of manganese than in the absence of manganese.

Finally, Applicant argues, as understood by the Examiner, that Tabor and Richardson actually teach away from the combination of Hardin and McGuigan because they show that manganese slows down the incorporation of base-labeled nucleotides, such as those used by McGuigan as compared to magnesium. This argument is not persuasive because McGuigan uses gamma phosphate-labeled nucleotides, i.e. terminal-phosphate-labeled nucleotides (pg. 31, col. 1, for example). Thus, a skilled artisan would have expected Sequenase to have the ability to utilize terminal-phosphate-labeled nucleotides in the presence of manganese.

Thus, the rejection is maintained.

New Grounds of Claim Rejections - 35 USC § 103

The following new grounds of rejections are made in view of previously considered prior art. Thus, the current Office Action is NON-FINAL.

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The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim(s) 8-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hardin (U.S. 2003/0064366 A1) in view of McGuigan et al. ("DNA fingerprinting by sampled sequencing" Methods Enzymol. 1993;218:241-58) as applied to claim 1 above, in further view of Tabor et al. ("Effect of manganese ions on the incorporation of dideoxynucleotides by bacteriophage T7 DNA polymerase and Escherichia coli DNA polymerase I" Proc Natl Acad Sci U S A. 1989 Jun;86(11):4076-80).

The teachings of the previously applied reference(s) have been outlined in the above rejections. The previously applied reference(s) do not expressly teach the presence of another metal salt other than manganese within the transfer reaction.

Tabor and Richardson teach that, in the presence of magnesium, Sequenase is highly processive (fig. 2; col. 1, middle, for example). Furthermore, they teach that, in the presence of manganese and magnesium, Sequenase continues to favor the incorporation of ddNTPs over dNTPs, as compared to the presence of only magnesium (table 1, for example). Therefore, sequencing reactions containing Sequenase in the presence of manganese as well as magnesium were well known at the time of invention, and shown to give reliable results.

Therefore, it would have been *prima facie obvious* a skilled artisan at the time of invention to incorporate manganese and magnesium ions into the methods of Hardin since such a reaction, as demonstrated by Tabor and Richardson, would have been expected to give a predictable result.

Conclusion

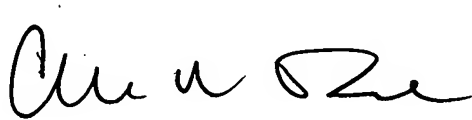
Claim(s) 1 and 4-12 are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Babic whose telephone number is 571-272-8507. The examiner can normally be reached on Monday-Friday 7:00AM to 4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

 9/4/07

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